[N-(3-Methoxypyridone-4)]-acetaldehyde.—3-Methoxypyridone-4, bromoacetal and potassium hydroxide were caused to react in the manner described for pyridone-4. More than 90% of the theoretical quantity of potassium bromide was formed. No attempts were made to isolate the acetal; instead, its aqueous solution was refluxed with hydrochloric acid. On neutralizing with sodium carbonate, the liquid turned a dark brown but no aldehyde separated. By reaction of the crude material with semicarbazide, however, a semicarbazone was formed; its yield indicated that the over-all yield of aldehyde, calculated on 3-methoxypyridone-4, was about 40%. The semicarbazone was recrystallized from water and dried over phosphorus pentoxide in the vacuum desiccator; m. p. 188–188.5° with decomposition.

Anal. Calcd. for $C_9H_{12}O_3N_4 \cdot 2H_2O$: C, 41.53; H, 6.20; N, 21.53; H_2O, 13.84. Found: C, 41.86; H, 6.30; N, 21.41; H_2O, 13.76.

The anhydrous compound, which may be prepared by drying over phosphorus pentoxide at 100° (1 mm.), is very hygroscopic.

Summary

(N-Pyridone-4)-acetaldehyde and [N-(3-methoxypyridone-4)]-acetaldehyde have been synthesized.

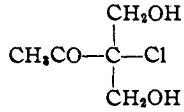
PITTSBURGH 13, PA. RECEIVED JULY 25, 1947

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF NORTHWESTERN UNIVERSITY AND COMMERCIAL SOLVENTS CORPORATION]

The Condensation of Chloroacetone with Formaldehyde

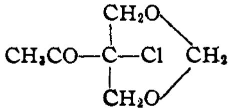
BY CHARLES D. HURD, WARREN D. MCPHEE[1] AND GLEN H. MOREY

While the condensation of formaldehyde with lower ketones has been studied extensively, the reaction of this aldehyde with chloroacetone has not previously been investigated. From the reaction of one mole of chloroacetone with 2.1 moles of formaldehyde, there are obtained three substances: A, a crystalline solid melting at 61–62°; B, a colorless oil distilling at 93.5° (10 mm.); C, a colorless oil distilling at 73–74.5° (10 mm.). From the evidence presented herein, it has been concluded that these substances are respectively 2-chloro-2-acetyl-1,3-propanediol, 2-chloro-2-acetyl-1,3-propanediol formal and 4-hydroxy-3,3-dichloro-2-butanone.



$$CH_3CO-\overset{\displaystyle CH_2OH}{\underset{\displaystyle CH_2OH}{C}}-Cl$$

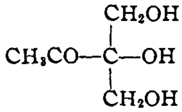
A



B

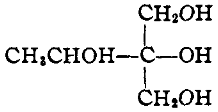
$CH_3COCCl_2CH_2OH$

C



$$CH_3CO-\overset{\displaystyle CH_2OH}{\underset{\displaystyle CH_2OH}{C}}-OH$$

D



$$CH_3CHOH-\overset{\displaystyle CH_2OH}{\underset{\displaystyle CH_2OH}{C}}-OH$$

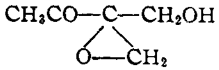
E

In determining the structure of substance A, it is apparent from the empirical formula that two hydroxymethyl groups have been introduced. It is necessary only to ascertain which α-carbon atom carries them. This was done by oxidation of A to acetic acid and by reaction with sodium hypoiodite with the formation of iodoform. ω-Chloroacetophenone is known to give a negative iodoform reaction,[2] and chloroacetone was found to give similar results. In view of these facts, A was assigned the structure shown.

Compound B differs from A only by the presence of one more carbon atom. It seemed logical that B should be the cyclic formal derived from A by reaction with a third mole of formaldehyde. Compound A was converted into B by means of dry formaldehyde in ether in the presence of a trace of acid, thus proving the structure of B. The compound so synthesized was shown to be identical with B.

The high chlorine content of C indicated that it was derived from dichloroacetone, which is generally present in small amounts in chloroacetone. Structure C, analogous to structure A, was selected because this compound gives a positive iodoform test. The formula was confirmed by synthesis of C from α,α-dichloroacetone and formaldehyde.

2-Chloro-2-acetyl-1,3-propanediol, A, was readily converted to its diacetate with ketene and to its dibenzoate with benzoyl chloride. Upon treatment with aqueous or alcoholic alkali, there is obtained a triol believed to be acetylglycerol, D. There is no evidence on the question whether this comes by direct saponification or by way of dehydrohalogenation to an ethylene oxide intermediate,



By the reaction of three moles of formaldehyde per mole of chloroacetone in the presence of one mole of sodium hydroxide, there is obtained substance D. The latter was identical with the triol obtained by alkaline hydrolysis of A. Substance D was reduced by sodium in alcohol to a tetrol, 2-hydroxymethyl-1,2,3-butanetriol, E.

Experimental

Reaction of Chloroacetone and Formaldehyde.—Chloroacetone (containing a little α,α-dichloroacetone) and formalin (40% solution) were mixed in a molar ratio of 1:2.1. The mixture was agitated at 25° for thirty minutes, during which time 2 *N* sodium hydroxide solution was added dropwise till 0.27 mole of the base was added. There was some heat of reaction during this addition, and the two-layer system gradually became homogeneous. The

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[1] Holder of Commercial Solvents Corporation Fellowship, 1938–1940.

[2] Fuson and Tullock, THIS JOURNAL, 56, 1638 (1934).

mixture was shaken three hours longer, then distilled. After the water was removed at 100°, colorless volatile products were collected at 140° (5–10 mm.). A non-volatile tarry residue (weighing 8–9% of the initial reactants) remained in the flask and the distillate was found to comprise a colorless, sirupy liquid and a crystalline solid which were separated by filtration. The liquid represented 21% of the initial reactants and the solid 33%. The latter was shown to be 2-chloro-2-acetyl-1,3-propanediol. It melted at 61–62° after crystallization from heptane.

Anal. Calcd. for $C_5H_9ClO_3$: Cl, 23.25; mol. wt., 152.5. Found: Cl, 23.36; mol. wt., 149.

Two components, both colorless oils, were separated from the sirupy liquid by distillation: component C, b. p. 73° (10 mm.), d^{20}_{20} 1.371; component B, b. p. 93.5° (10 mm.), d^{20}_{20} 1.286.

Anal. of B. Calcd. for $C_6H_9ClO_3$: Cl, 21.57. Found: Cl, 21.45.

Haloform Reactions.—2-Chloro-2-acetyl-1,3-propanediol (A) was tested as follows:

Five-tenths gram of the substance was dissolved in a solution formed by adding 1.25 g. of iodine to 8 ml. of 10% sodium hydroxide solution, after which 1.25 g. of iodine was added in small amounts with sufficient alkali solution to discharge the brown color. A voluminous white precipitate of iodoform (2 g. or 78%) was formed, m. p. 119°.

In a similar way (A) gave a positive chloroform test by the following procedure: Ten cubic centimeters of 10% sodium hydroxide solution was saturated at 0° with chlorine, followed by addition of 10 cc. more alkali and 1 g. of substance A. The mixture was distilled and the distillate contained an oily layer of chloroform, which was separated and dried; n^{20}_D 1.4458.

4-Hydroxy-3,3-dichloro-2-butanone (C) gave iodoform positively by the above procedure using 1 ml. of C; yield 0.4 g. (25%), m. p. 118.5–119°.

2-Chloro-2-acetyl-1,3-propanediol diacetate (0.5 g.) gave a low yield of impure iodoform by mixing it with 5 ml. of sodium hypoiodite solution prepared by dissolving 2.5 g. of iodine in 16 ml. of 10% sodium hydroxide. The resulting suspension was shaken for fifteen minutes, during which time about 0.1 g. of iodoform melting at 114° was obtained.

Chloroacetone gave a negative iodoform test as follows: 0.6 ml. of chloroacetone was shaken for ten minutes with 8 ml. of sodium hypoiodite solution prepared as above. No iodoform was obtained.

Oxidation of 2-Chloro-2-acetyl-1,3-propanediol.—A sample of the 2-chloro-2-acetyl-1,3-propanediol weighing 1.505 g. (0.00986 mole) was dissolved in 100 g. of water and oxidized quantitatively by means of a chromic acid mixture prepared from 8.8 g. (0.03 mole) of potassium dichromate, 75 g. of water and 22 ml. of concentrated sulfuric acid. The mixture was refluxed in an all-glass apparatus until the evolution of carbon dioxide ceased (thirty minutes). It was then distilled slowly until crystals separated, whereupon 100 g. of water was added, and the distillation was continued. The combined distillate and washings were made up to 500 ml. and two 25-ml. samples were titrated with 0.0651 *N* sodium hydroxide. The ml. of alkali required were 5.36 and 5.34, respectively, representing a total of 0.00697 mole of acid distilled. This is 0.71 mole of acid per mole of 2-chloro-2-acetyl-1,3-propanediol oxidized. The sodium salt, obtained by evaporating the neutralized distillate, was converted into the *p*-bromophenacyl acetate, m. p. 85°.

Duclaux constants were taken on a fresh portion of the distillate: 6.0, 6.4, 6.8. These check fairly well with those for acetic acid, 6.8, 7.1, 7.4.

Conversion of 2-Chloro-2-acetyl-1,3-propanediol into its Formal.—Five grams of dry paraformaldehyde in a 125-cc. flask was heated to 170–180° in an oil-bath while a slow stream of nitrogen (dried with concentrated sulfuric acid) was passed through the flask. The outlet tube (12 mm.) led into a test-tube containing 30 ml. of anhydrous ether at −80°. The heating was continued until nearly all the polymer had disappeared. The gain in weight of the ether solution was 1.3 g., representing 0.04 mole of formaldehyde. To this cold (−80°) solution was added 2.2 g. (0.014 mole) of 2-chloro-2-acetyl-1,3-propanediol (A) and two drops of concentrated sulfuric acid. The solution was kept at −80° for twelve hours, then allowed to come to room temperature. After two days the ether was evaporated on the steam-bath. About 2.3 g. of colorless oil was left. This represents about a 95% yield of the cyclic acetal. The oil was not soluble in water, whereas the starting products were.

The 2,4-dinitrophenylhydrazones of the oil and of substance B (b. p. 93.5° at 10 mm.) both melted at 159–160° after recrystallization from alcohol. Their mixture also melted at 159–160°, but if either was mixed with formaldehyde 2,4-dinitrophenylhydrazone (m. p. 163°), the m. p. was depressed to 139–150°. Hence, the hydrazone is not that of formaldehyde. 2-Chloro-2-acetyl-1,3-propanediol, the starting product, gives no 2,4-dinitrophenylhydrazone when prepared in alcohol, since the hydrazone is soluble in alcohol.

Condensation of α,α-Dichloroacetone with Formaldehyde.—A mixture of 51 g. of α,α-dichloroacetone (55.01% Cl) and 65 ml. of 40% formalin was stirred mechanically while 5 g. of dry sodium carbonate was added slowly. After the initial vigorous reaction (the solution boils) the mixture was stirred at room temperature for eight hours. The lower organic layer was separated, dried with drierite, filtered and vacuum-distilled. The odor of formaldehyde was noticeable. A small forerun (4.5 g.) was obtained, b. p. 78–81° (20 mm.), n^{20}_D 1.4725, after which the main body of 4-hydroxy-3,3-dichloro-2-butanone was obtained, b. p. 81° (20 mm.), 105° (50 mm.), d^{20}_{20} 1.34, n^{20}_D 1.4727. There was no other volatile fraction. This product has the same physical constants as substance C (b. p. 79.5–80.5° (20 mm.), n^{20}_D 1.4724), isolated originally from the experiment with chloroacetone. These directions were modified for runs involving several kg. of product with yields consistently at about 75%.

Anal. Calcd. for $C_4H_6Cl_2O_2$: Cl, 45.21. Found: Cl, 44.96.

The semicarbazone of this substance melted with decomposition at 230–231° after recrystallization from alcohol. The semicarbazone of C, similarly prepared, also melted at 229–230°. The mixed m. p. of the two was 229–230°.

Esters of 2-Chloro-2-acetyl-1,3-propanediol

Diacetate.—This was made by passing a slight excess of ketene into an acetone solution of the diol. From 2 g. of (A), 1.5 g. of 2-chloro-2-acetyl-1,3-propanediol diacetate, b. p. 138–143° (18 mm.), was obtained.

Anal. Calcd. for $C_9H_{13}ClO_5$: Cl, 15.0. Found: Cl, 14.7.

Dibenzoate.—Reaction with boiling benzoyl chloride effected benzoylation in 85% yield. Crystallization was from ethanol or ligroin: m. p., 82–83°.

Anal. Calcd. for $C_{19}H_{17}ClO_5$: Cl, 9.84. Found: Cl, 10.0.

Bis-*p*-nitrobenzoate.—Treatment with *p*-nitrobenzoyl chloride and pyridine (boiling), and crystallization from ethyl acetate (or ethanol) resulted in a 36% yield, m. p. 161°.

Anal. Calcd. for $C_{19}H_{15}ClN_2O_9$: Cl, 7.89. Found: Cl, 8.11.

Acetylglycerol from (A).—Five grams of the solid 2-chloro-2-acetyl-1,3-propanediol was dissolved in 100 ml. of 95% ethanol containing 2.5 g. of potassium hydroxide. A precipitate of potassium chloride formed immediately. The mixture was neutralized with a solution of hydrogen chloride in absolute alcohol. The salt was filtered off and washed with absolute alcohol. The alcohol was removed at 20 mm. by heating in a bath at 60°. The residual yellow sirup was not distillable at 5 mm. from a Claisen flask with a bath temperature of 175°, but it distilled readily from a simple molecular still[3] connected to a pair of mercury pumps and heated by a bath at 120–125°. The colorless, non-viscous, water-soluble distillate (D_1) weighed 1.8 g.

Material possessing the same properties was obtained by treatment with an equivalent of aqueous (6 *N*) sodium hydroxide, removal of water by vacuum distillation, filtration to remove sodium chloride, and distillation from the molecular still. The liquid will be called D_2.

From Chloroacetone.—Five grams (0.055 mole) of chloroacetone and 0.16 mole of formaldehyde (as formalin) were mixed and maintained at 20° while 0.055 mole of 6 *N* sodium hydroxide solution was added little by little with stirring in the course of a day. The mixture was then heated to 60° for ten hours to consume the base. The water was removed by evaporation under reduced pressure up to 90° and sodium chloride was precipitated in quantitative yield. The sirupy material (6.5 g.) was not distillable in an ordinary Claisen flask up to 175° (bath) and 5 mm., but it came over readily from a molecular still with the conditions specified above. The limpid distillate, to be referred to as D_3, weighed 1.5–2 g. There was a red-brown, non-volatile residue in the still.

Anal. Calcd. for $C_5H_{10}O_4$: active hydrogen atoms, 3. Found (Zerewitinoff): active hydrogen atoms from D_1, 3.13, 3.09; from D_3, 3.06, 2.98.

p-Bromobenzoic Ester.—A mixture of 0.5 g. of acetylglycerol, 4 g. of p-bromobenzoyl chloride and 30 ml. of dry pyridine was maintained at 0° for thirty-six hours, and subsequently treated with 40 ml. of 5% sodium carbonate solution for eight more hours at 0°. Fifty grams of water was added, and the mixture was filtered. The acetylglycerol tris-p-bromobenzoate was digested in ethanol and recrystallized from butyl ether; yield of white needles, 2 g. (79%). D_1, D_2 and D_3 all behaved identically, giving products melting at 215–216°. Mixed melting point determinations of these products were not lowered.

The same product was formed but in lower yield if a reaction temperature of 100–115° was maintained.

Anal. Calcd. for $C_{26}H_{19}Br_3O_7$: Br, 35.1. Found: Br, 35.9.

Reduction of Acetylglycerol.—Four grams of acetylglycerol was dissolved in 17 ml. of ethanol and 3 g. of water. Two grams of sodium was added in small pieces during two hours. At first, the mixture was cooled with ice; when the reaction became less vigorous, it was allowed to proceed at room temperature. After ninety minutes the reaction was very slow, so 10 ml. more of alcohol was added. The solution became a deep red and a yellow precipitate formed. After the sodium had been added, the mixture was neutralized with a saturated solution of dry hydrogen chloride in alcohol. The solution was filtered from the salt which precipitated, the solvent was removed, and the 5 cc. of dark residue was distilled in the molecular still with a bath temperature of 80–85°. The yield of colorless distillate was 0.91 g. or 23%.

Anal. Calcd. for $C_5H_{12}O_4$: active hydrogen atoms, 4. Found (Zerewitinoff): active hydrogen atoms, 3.84, 4.02.

Summary

Formaldehyde condenses with chloroacetone to yield 2-chloro-2-acetyl-1,3-propanediol and its cyclic formal. α,α-Dichloroacetone, similarly treated, gives rise to 4-hydroxy-3,3-dichloro-2-butanone. Various reactions of these compounds are developed.

EVANSTON, ILLINOIS
TERRE HAUTE, INDIANA
RECEIVED AUGUST 4, 1947

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[3] Hickman and Sanford, *J. Phys. Chem.*, **34**, 643 (1930).

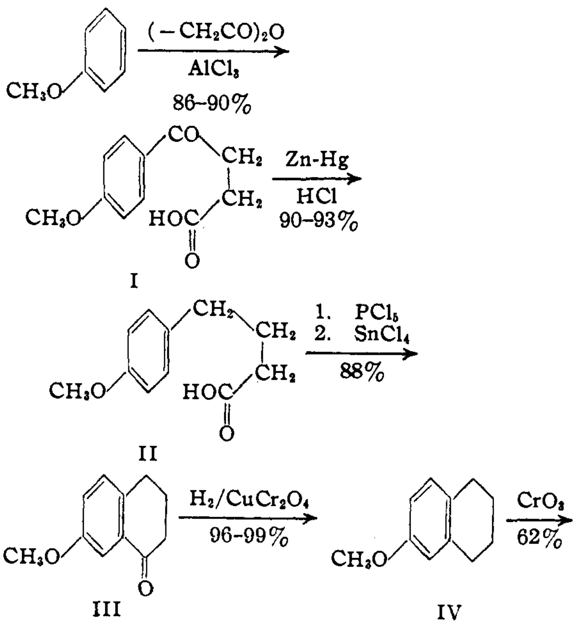
[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF THE UPJOHN COMPANY]

6-Methoxy-1-tetralone

BY DONALD G. THOMAS AND ALAN H. NATHAN

Of the various methods[1-6] described for the synthesis of 6-methoxy-1-tetralone (V), the one most generally used is that based on the chromic acid oxidation[5] of 6-methoxytetralin (IV), which usually has been obtained from tetralin by sulfonation, alkali fusion and methylation.[7,8] The over-all yield of 6-methoxy-1-tetralone by this method is about 30–35%.

An alternate route to 6-methoxy-1-tetralone is outlined below, and by this procedure we have obtained 6-methoxy-1-tetralone in over-all yields of 40–45%.



The reaction between anisole and succinic an-

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[1] Thompson, *J. Chem. Soc.*, 2310 (1932).

[2] Robinson and co-workers, *ibid.*, 1285, 1288 (1935); 192, 747 (1936); 1581 (1937).

[3] Chuang and Huang, *Ber.*, **69**, 1505 (1936).

[4] Martin, THIS JOURNAL, **58**, 1438 (1936).

[5] Burnop, Elliott and Linstead, *J. Chem. Soc.*, 727 (1940).

[6] Bachmann and Thomas, THIS JOURNAL, **64**, 94 (1942).

[7] Schroeter, *Ann.*, **426**, 83 (1922).

[8] Since this manuscript was submitted for publication, details of a superior method for the preparation of 6-methoxytetralin by catalytic hydrogenation of β-naphthyl methyl ether have been published by Stork, THIS JOURNAL, **69**, 576 (1947).